(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
6 January 2005 (06.01.2005)

PCT

(10) International Publication Number
WO 2005/000384 A1

(51) International Patent Classification[7]: A61M 5/315, 5/20

(21) International Application Number: PCT/US2004/017959

(22) International Filing Date: 7 June 2004 (07.06.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/476,365 5 June 2003 (05.06.2003) US

(71) Applicant *(for all designated States except US)*: **UNIVERSITY OF FLORIDA** [US/US]; 223 Grinter Hall, Gainesville, FL 32606-5500 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **BOZEMAN, William** [US/US]; 5340 Mercia Court, Winston-Salem, NC 27106 (US). **LUTEN, Robert, C.** [US/US]; 14710 Plumosa Drive, Jacksonville, FL 32250 (US).

(74) Agents: **EFRON, Margaret** et al.; Saliwanchik, Lloyd & Saliwanchik, A Professional Association, PO Box 142950, Gainesville, FL 32614-2950 (US).

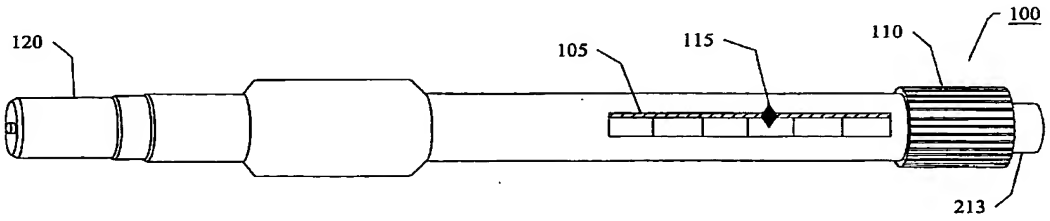
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AUTO-INJECTION DEVICES AND METHODS FOR INTRAMUSCULAR ADMINISTRATION OF MEDICATIONS



(57) Abstract: The present invention provides auto-injection devices for the administration of appropriate medication dosage and needle-depth penetration based on a patient's relevant parameters. In one embodiment, the auto-injection device of the present invention comprises non-volumetric indicia based upon a patient parameter for use in selecting the appropriate medicament dosage for administration to the patient. In another embodiment, the non-volumetric indicia not only provides appropriate medicament dosage but also appropriate needle depth penetration.

WO 2005/000384 A1

DESCRIPTION

AUTO-INJECTION DEVICES AND METHODS FOR INTRAMUSCULAR ADMINISTRATION OF MEDICATIONS

Cross-Reference to a Related Application

This application claims the benefit of U.S. provisional patent application Serial No. 60/476,365, filed June 5, 2003.

Background of Invention

There are a variety of injection devices available for delivering medication to a patient, the most typical device being the syringe. With traditional syringes, a user must calculate the correct amount of medication needed for the patient based on a number of parameters (*i.e.*, age, height, and weight) as well as the correct needle size and depth necessary for appropriate injection of medication into the patient. Once the appropriate dosage and needle requirements have been calculated, the user attaches the appropriate needle to the syringe and inserts the needle into a separate medication vial to withdraw an appropriate medication dose. Once the medication is withdrawn from the vial, the user removes any air bubbles and extra medication, and then injects the medication into the patient at an appropriate depth.

Unfortunately, medication error and/or adverse drug events may result due to errors in professional practice/judgment, health care products, procedures, and systems including, for example, errors in prescribing, order communication, product labeling, packaging, and nomenclature. Medication errors or adverse drug events can include noxious and undesired effect of a drug due to inappropriate medication dosage.

Several studies have demonstrated the high incidence of medication errors and the sometimes fatal results. For example, a death certificate study found a greater than two-fold increase in deaths caused by medication errors between 1993, during which 7,391 people died, and 1983, when 2,876 patients died from medication errors,

see Phillips, D. P., *et al.*, "Increase in U.S. Medication-Error Deaths Between 1983 and 1993," *Lancet*, (1998), 351(9103). Another report estimates 6.5 adverse drug events per 100 admissions, as well as an additional cost of $2,000 per adverse drug event, for a hospitalized patient, excluding malpractice costs or the cost of injury to the patient. Furthermore, while most adverse drug events result from errors at the ordering stage, many occurred at the administering stage. See Bates, D. W., *et al.*, "Incidence of Adverse Drug Events and Potential Adverse Drug Events," *JAMA*, (1995), 274(1):29-30.

With regard to pediatric treatments, a four-year study that investigated patterns of medication errors in neonatal and pediatric intensive care-units found an error rate of 14.7% with one medication error occurring for every 6.8 admissions. The study found that while the percentage breakdown varied, all health care providers: physicians, nurses, and pharmacists, were responsible, see Raju T N K, *et al.*, "Medication Errors in neonatal and pediatric intensive care units," *Lancet*, (1989), 374-376.

Thus, typical syringes, which require a user to calculate the correct amount of medication needed for a patient based on a number of parameters (*i.e.*, age, height, and weight), do not aid in reducing the incidence of medication errors or adverse drug events. Further, these syringes suffer from many drawbacks. For instance, since they are not typically preloaded with medication, the user must carry a separate medication vial. Moreover, people with dexterity disorders often have difficulty lining up the needle portion of the syringe with the rubber septum on the medication vial. This can lead to unintentional needle pricks or excessive time being required to complete an injection, both of which tend to inhibit compliance with a medical regimen. Also, it is often difficult for children or people with failing eyesight to line up the medication with the proper dosage line on the outer casing of the syringe.

As an alternative, automatic injection apparatuses have been developed. An automatic injection enables an individual to self-administer a dosage of liquid medication into his or her flesh. The advantage of automatic injectors is that they contain a measured dosage of a liquid medication in a sealed sterile cartridge, which can be utilized for delivering the medication into the flesh during emergency situations (*i.e.*, such injectors can carry antidotes for nerve gas, insulin for diabetes, or

epinephrine for allergic reactions). Another advantage of automatic injectors is that the self-administration of the medication is accomplished without the user initially seeing the hypodermic needle through which the medication is delivered and without having the user manually force the needle into his or her own flesh. Examples of such known injectors are disclosed in U.S. Patent Nos. 5,085,641; 5,540,664; 5,569,192; and 5,092,843.

A typical drawback of automatic injectors is that they administer a single, one-time dose of medication and are not re-usable. After this single use, the entire apparatus is discarded. This results in high cost and waste of medical equipment.

Another drawback is the relatively short storage life of some medications. The storage life of a medication is generally less than the useful life of the automatic injection apparatus. Automatic injectors can be stored for long periods of time, often 5 years or more. Unfortunately, many medications do not have a comparable storage life. For example, some medications have storage lives of 1-2 years or less. Thus, the medicine could become ineffective before the injector is used, resulting in the wasteful disposal of unused injection apparatuses. This also contributes to high costs.

Even with the means for automatic injection, many of these injection devices still require the user to measure dosage and needle injection depth, which is time consuming and requires an appropriate knowledge base and proper instruments and accessories. Moreover, most automatic injection devices are designed for single use administration to an adult. In emergent situations, it is not feasible to use injection devices of this type on all patients. For example, where a toxic agent has been released, providing an adult dosage amount of an antidote to toxic agents to a small child could harm or even kill the child. Thus, current auto-injection devices would not be available as treatment for about 20% of the current population (children account for roughly 20% of the population) during emergent situations.

Accordingly, it is highly desirable that an injection device be provided that can automatically, efficiently, and appropriately administer medicaments, and which can easily and rapidly be adjusted to administer the appropriate dosage to any patient. Many past devices have failed to provide convenience, accuracy, and efficiency in delivering medicaments to patients of various sizes and ages. Thus, current injection devices have been less than satisfactory.

Brief Summary

The present invention provides auto-injection devices for administration of medication to a patient or via an intravenous line. The devices of the subject invention have a dosage adjusting means and a needle depth adjusting means. In one embodiment, the auto-injection device also has an adjustment mechanism that simultaneously sets the dosage adjusting means and the needle depth adjusting means based on certain patient parameters. These parameters could include, for example, the age, size, weight, and gender of the patient. A particularly advantageous aspect of the devices and methods of the subject invention is their ease of use with both adult and pediatric patients.

According to the present invention, a variety of medicaments can be administered using the subject devices. For example, liquid medications can be integrally stored within the device interior and subsequently administered. Alternatively, the device of the subject invention can readily deliver medications that are provided in solid formulations that require a solvent.

In one embodiment of the present invention, an auto-injection device has a dosage adjusting means, an/or a needle depth adjusting means, an adjustment mechanism, and a reconstitution mechanism. The auto-injection device also has a means for separating different substances from contact until such time as needed for administration. At such time, the reconstitution mechanism is activated to mix the different substances together and allow for proper medication dosage and injection. The auto-injection device has two chambers created and separated by a dividing piston that includes upper and lower plungers. Distally, the lower plunger seals the upper or liquid chamber. The lower or dry drug chamber can be separated from the diluent liquid by an internal hydrophobic membrane that allows air but not water to pass through it.

In use, after removal of the auto-injection device from its packaging, the operator, which may be a patient, can manipulate the adjustment mechanism to select the appropriate indicia of dosage and needle depth. The readily recognizable indicia are based on, and correspond to, an individual's relevant parameters (*i.e.*, gender, age, height, or weight). The indicia are not volumetric. In other words, unlike a standard syringe, which would typically show milliliters, the devices of the subject invention

give an indication of dosage and/or needle depth. Thus, the non-volumetric indicia listed on the auto-injection device correspond to appropriate dosages and/or needle injection depth based on the patient's characteristics. The indicia may be based on colors, numbers, or some other easily-identifiable system.

The adjustment mechanism can utilize a variety of known adjustors including, but not limited to, a dial or slide. Concurrent with the movement of the adjustment mechanism, an indicator provides notice to the user of the non-volumetric indicia chosen for the appropriate dosage and/or needle injection depth to be administered.

In a specific embodiment, the indicator is located within a slot in the side of the auto-injection device. Disposed along the sides of the slot are indicia indicating dosage and needle-depth selection based on specific patient parameters. Contemplated indicia include, but are not limited to, a color-coded measurement system. An example of a color-coded measurement system includes a Broselow-Luten tape.

One embodiment of the subject invention provides a method for using an auto-injection device having an adjustment mechanism that adjusts the amount of medicament to be delivered based on specific patient parameters (*i.e.*, patient size). The device is set for an individual's parameter and a protective cover, if used, is removed. The distal end of the device is applied to an appropriate body area for intramuscular injection of the medicament. In a preferred embodiment, the subject device is used to administer a medicament to the thigh or gluteal muscle of a patient. Firm pressure is applied to the auto-injection device so that a trigger, located in the distal end of the device, is actuated. Actuation of the distal end of the device in turn actuates a spring-loaded injector mechanism to advance a sterile needle into the patient's body and to inject the chosen volume of liquid medication. In another embodiment, a trigger located at the proximal end of the device can actuate the spring-loaded injector mechanism to advance the needle into the patient's body and inject the chosen volume of medication.

In another embodiment, the injection device of the subject invention can administer proper medication dosage to an intravenous line.

In another embodiment, the adjustment mechanism adjusts the depth of the needle penetration based on specific patient parameters (*i.e.*, patient age). In yet

another embodiment, the adjustment mechanism simultaneously adjusts the amount of medicament delivered and the depth of the needle penetration based on specific patient parameters (*i.e.*, patient size and age).

Another embodiment of the subject invention provides an adjustment mechanism that can be dialed up or down without limitation. In another embodiment, the auto-injection device of the subject invention has a means for locking the adjustment mechanism in a selected position either before or when the trigger of the device is actuated and injection of the medicament into the patient occurs.

A further embodiment provides a device for pediatric patients requiring medicaments prior to the establishment of intravenous access.

Brief Description of Drawings

Figure 1 is a schematic diagram of an injection device for administering liquid medicaments in accordance with the present invention.

Figure 2 is a longitudinal section view of the device shown in Figure 1.

Figure 3 is a schematic diagram of an auto-injection device for dispensing reconstituted dry medicaments in accordance with the present invention.

Figure 4 is a longitudinal section view of the device shown in Figure 3.

Detailed Disclosure

The present invention provides auto-injection devices for administration of medication. In a preferred embodiment, the auto-injection device has a dosage adjusting means, a needle depth adjusting means, and an adjustment mechanism. These aspects of the invention provide an auto-injection device that easily and automatically administers the appropriate medication dose and/or needle-depth penetration to all patients, including adults and children, based on specific patient parameters.

In a preferred embodiment, the adjustment mechanism simultaneously establishes the setting for the dosage and the needle depth. A variety of medicaments can be administered using the subject device, including solid formulations/solvent or liquid medications integrally stored within the device interior.

In use, after removal of the auto-injection device from its packaging, the operator, which may be a patient, can actuate the adjustment mechanism to select the appropriate settings (as shown by easily recognized non-volumetric indicia) that corresponds to an individual patient's relevant parameter(s) (*i.e.*, age, height, weight). The adjustment mechanism can utilize a variety of known adjustors including, but not limited to, a dial or slide. In one embodiment, concurrent with the movement of the adjustment mechanism, an indicator moves within a slot in the side of the auto-injection device. Disposed along the sides of the slot are indicia representing the appropriate dosage and needle-depth selection for an individual patient. Contemplated indicia include, but are not limited to, a color-coded measurement system. An example of a color-coded measurement system includes a Broselow-Luten tape.

The terms "non-volumetric indicia" or "parameter indicia" as used herein, refer to displays/markings that represent the amount of medication to be administered and/or the appropriate needle-depth penetration. Non-volumetric indicia (as opposed to known volumetric indicia, *i.e.*, mL) can include numbers, characters, or colored markers. For example, non-volumetric indicia can include a series of different colors (*i.e.*, red, orange, yellow). Each of the colors represents the appropriate needle-depth penetration and/or amount of medication that should be administered to an individual based on the individual's parameters (*i.e.*, age, height, weight, or gender).

The term "individual" or "patient" includes animals of avian, mammalian, or reptilian origin. Mammalian species that can benefit from the methods and devices of the subject invention include, but are not limited to, apes, chimpanzees, orangutans, humans, monkeys; dogs, cats, guinea pigs, and mice.

In one embodiment, an auto-injection device of the present invention includes an adjustment mechanism that adjusts the amount of medicament to be delivered based on an individual patient's parameters (*i.e.*, patient size). In use, the device is set for the individual's parameter and a protective cover, if used, is removed. The distal end of the device is applied to an appropriate body area for intramuscular injection of the medicament. In a preferred embodiment, the subject device is used to administer a medicament to the thigh or gluteal muscle of a patient. Firm pressure is then applied to the auto-injection device so that a trigger, located in the distal end of the

device, is actuated. Actuation of the distal end of the device in turn actuates a spring-loaded injector mechanism to advance a sterile needle into the patient's body and to inject the chosen volume of liquid medication.

In another embodiment, the injection device of the subject invention is used to administer the proper dosage of medication to an intravenous line.

In another embodiment, a trigger located at the proximal end of the device can actuate the spring-loaded injector mechanism to advance the needle into the patient's body and inject the chosen volume of medication.

Another embodiment of the subject invention has an adjustment mechanism that adjusts the depth of the needle penetration based on an individual's parameters (*i.e.*, patient age). Again, after the device has been set for the individual's parameter, a protective cover, if used, is removed and the distal end of the device is applied to an appropriate body area for intramuscular injection of the medicament, wherein the needle depth penetration is appropriate based on the patient's parameter.

In yet another embodiment, the adjustment mechanism simultaneously adjusts the amount of medicament delivered and the depth of the needle penetration based on an individual patient's parameters.

A further embodiment provides an auto-injection device having an adjustment mechanism that can be dialed up or down without limitation. In another embodiment, the auto-injection device of the subject invention has a means for locking the adjustment mechanism in a selected position either before or when the trigger in the proximal end of the device is actuated.

A further embodiment provides a device for pediatric patients requiring medicaments prior to the establishment of intravenous access.

The following examples and accompanying figures describe specific embodiments of the device and methods of the present invention, and features thereof. With regard to means for fastening, mounting, attaching, or connecting the components of the present invention to form the device as a whole, unless specifically described otherwise, such means are intended to encompass conventional fasteners such as threaded connectors, snap rings, clamps such as screw clamps and the like, rivets, toggles, pins, and the like. Components may also be connected by adhesives, glues, welding, ultrasonic welding, and friction fitting or deformation, if appropriate.

Unless specifically otherwise disclosed or taught, materials for making components of the present invention may be selected from appropriate materials such as metal, metallic alloys, natural and manmade fibers, vinyls, plastics, and the like, and appropriate manufacturing or production methods including casting, extruding, molding, and machining may be used.

References to front and back, right and left, top and bottom, and upper and lower are intended for convenience of description, not to limit the present invention or its components to any one positional or special orientation.

The auto-injection devices, as disclosed in U.S. Patent Nos. 6,290,679; 6,193,698; 5,569,192; 5,540,664; 5,141,496; and 5,104,380, may be modified consistent with the teachings provided herein for use according to the subject invention. Specifically, the auto-injection devices of the subject invention have one or more of a dosage adjusting means, a needle depth adjusting means, and an adjustment mechanism.

Example 1 — Liquid Medicaments

As illustrated in Figure 1, an auto-injection device **1** in accordance with the present invention is provided. The device **1** has non-volumetric indicia **5** that correspond to medication dosages based on an individual's relevant parameters. The appropriate dosage, which can be adjusted continuously or discretely, are marked on a non-volumetric scale (*i.e.*, Broselow-Luten tape) affixed to the housing of the device **1**. By rotating an adjustment knob **10** around its longitudinal axis, a user can select the appropriate dose of medication to be administered and/or needle penetration depth based on the patient's relevant parameters. A movable indicator **15** displays to the user a representation of the relevant parameter and appropriate dosage amount to be administered using the subject device **1**. The movable indicator **15** corresponds in movement to that of the adjustment knob **10**. A needle protector **20** is provided to protect the user from accidental needle punctures.

In this embodiment, the adjustment knob **10** actuates a dosage adjusting means and/or a needle depth adjusting means. In one embodiment, the adjustment knob **10** also operates as the dispensing button. The dosage to be administered and/or needle penetration depth is represented by the indicator **15**. The needle depth adjusting

means adjusts the depth to which the needle will penetrate the dermis of the patient during administration of the medication using the subject device **1**.

Figure 2 illustrates a longitudinal cross-section of an automatic injection device **1** of the subject invention. The device **1** comprises an elongated housing, including a distal enclosure **25** for accommodating a container of medication **30** and a needle **35**, and a proximal enclosure **40**. The proximal enclosure **40** accommodates a piston **45**, to which is attached the movable indicator **15**. Movement of the piston **45** in the direction of the medication container **30** outlet via the needle **35** displaces the medication.

The movement of the piston **45** (and moveable indicator **15**) is caused by contact pressure of a threaded rod **50**. The threaded rod **50** forms the driven member of a spindle drive, configured to include the threaded rod **50** and a threaded sleeve **55**. The threaded sleeve **55** surrounds the threaded rod **50** as the drive member. To move the piston **45**, the threaded sleeve **55** together with the threaded rod **50** is advanced against an elastic return force by actuation of the adjustment knob **10**. The adjustment knob **10** in turn actuates the piston **45** to advance in the direction toward the distal end of the proximal enclosure **40**. The adjustment knob **10**, the drive members **50, 55** and the piston **45** are linearly shifted along a common axis, the shifting axis, as indicated as a dot-dash in the figures. In this arrangement, the distance by which the adjustment knob **10** and the drive members **50, 55** are shifted on actuation is always the same. Thus, the distance covered by the piston **45**, as influenced by the drive **50, 55**, allows for variable selection of a dose of medication to be administered by injection.

The adjustment knob **10** comprises a sleeve part **70**, closed off by an exchange part **75**. The sleeve part **70** of the adjustment knob **10** protrudes through a proximal enclosure **40**. In the region of the sleeve part **70**, the adjustment knob **10** is connected to the threaded sleeve **55** by an anti-rotation lock. Thus, rotating the adjustment knob **10** automatically engages in rotation the threaded sleeve **55** around its longitudinal axis. The threaded rod **50** is linearly guided secured against rotation so that a rotation of the threaded sleeve **55** automatically results in a linear shift of the threaded rod **50**. At its proximal end facing the piston **45**, the threaded rod **50** comprises a flange or plunger **60**, with which it advances the piston **45** in the medication container **30** on actuation of the adjustment knob **10**. The shifting path of the threaded rod plunger **60**

is the same in length for each injection. Advancement is made against the elastic restoring force of a compression spring **65**, disposed between an appendage of the proximal enclosure **40** and a corresponding companion appendage on the threaded sleeve **55**. The compression spring **65** attempts to push back to its distal position the "actuating means," essentially consisting of the threaded sleeve **55**, threaded rod **50**, and the adjustment knob/dispensing button **10**.

The adjustment knob **10** comprises axially extending ridges and furrows **70** arranged uniformly distributed about the circumference of an outer shell surface of the adjustment knob **10** to ensure user grip of the adjustment knob **10**.

In one embodiment, the non-volumetric parameter indicia correspond to medication dosages and needle penetration depths based on an individual's height. The non-volumetric parameter indicia comprises a variety of colors that are found on a Broselow-Luten tape. The colors on a Broselow-Luten tape correspond to the appropriate medication dosage and needle penetration depth based on an individual's height. By way of example, where the medication is atropine to be used as an antidote to a nerve agent, non-volumetric parameter indicia of the color pink corresponds to the dosage of 0.32 mL of atropine and needle depth of 1/2 to 7/8 inch for a patient less than 76 cm in height.

In another embodiment, the non-volumetric parameter indicia correspond to medication dosages based on an individual's weight. The non-volumetric parameter indicia comprise a variety of characters corresponding to a dosage based on an individual's weight. By way of example, where the medication is atropine to be used as an antidote to a nerve agent, non-volumetric parameter indicia of 3 kg corresponds to a dosage of 0.12 mL of atropine (IV/IM 0.1mg/mL concentration) for an individual weighing 3 kg. Non-volumetric parameter indicia of 4 kg correspond to the dosage of 0.2 mL of atropine (IV/IM 0.1mg/mL concentration) for a patient that weighs 4 kg.

In another embodiment, the non-volumetric parameter indicia correspond to needle penetration depth based on an individual's height. The non-volumetric parameter indicia comprises a variety of colors that are found on a Broselow-Luten tape. The colors on a Broselow-Luten tape correspond to the appropriate needle depth penetration based on an individual's height. By way of example, non-volumetric

parameter indicia of the color pink corresponds to the needle depth of 1/2 to 7/8 inch for a patient less than 76 cm in height.

Example 2 — Solid/Solvent Medicament Mixtures

Another embodiment of the subject invention provides an auto-injection device for dispensing dry or unstable medications that require reconstitution prior to administration to a patient. The auto-injection device, as described in U.S. Patent Nos. 5,971,953 5,393,326; 4,983,164; 4,413,991; 4,202,314; and 4,214,584, may be modified consistent with the teachings provided herein for use according to the subject invention.

According to the subject invention, the auto-injection device has a dosage adjusting means, and/or a needle depth adjusting means, an adjustment mechanism, and a reconstitution mechanism. The reconstitution mechanism has two chambers created and separated by a dividing piston that includes upper and lower plungers. Distally, the lower plunger seals the upper or liquid chamber. The lower or dry drug chamber can be separated from the diluent liquid by an internal hydrophobic membrane that allows air but not water to pass through it. The auto-injection device of the subject invention is generally cylindrically shaped, having proximal and distal end portions. A middle section of the auto-injection device is of an enlarged diameter.

A bore extends between the proximal and distal end portions, the bore including upper and lower chamber sections for containing medicine contents to be dispensed including an upper liquid component and a lower dry medicinal component. A dispensing needle at the distal end of the housing can be provided for receiving the medicine contents of the lower chamber after mixing.

A pair of pistons is provided that are separately movable. A lower piston occupies the position in between the ends of the auto-injection device, and in between the upper and lower chambers. The lower piston is movable between upper and lower positions. An upper piston is positioned at the proximal end of the housing and slides within the bore during use.

The enlarged diameter middle portion of the barrel of the auto-injection device carries one or a plurality of longitudinally extending channels. These channels are

positioned at the middle of the housing and form a connection between the upper and lower chambers. The floating chamber has a maximum sidewall dimension that is less than the length of the channel or channels. The channels can therefore convey fluid in between the proximal and distal ends of the syringe and in between the upper and lower chambers when the first piston occupies a position adjacent the longitudinal channels and the ends of each channel extend beyond the ends of the lower piston.

The lower piston forms a seal to retain the liquid contents of the upper chamber away from the lower chamber when the first piston is in the upper position. The lower piston forms a seal that seals the combined liquid and dry contents from the channels prior to dispensing and after the liquid and dry medicinal portions have been reconstituted.

In accordance with the present invention, a dual chambered auto-injection device contains longitudinally extending bypass channels. These longitudinal channels are part of an enlarged middle diameter section of the auto-injection device, so designed in depth and width as to facilitate thorough mixing of all pharmaceuticals.

The advantage is obtained by the mixing channels being critically placed to begin and end generally equidistant from each end of the syringe so as to permit the lower chamber to accept and instantly retain a predetermined volume of diluent contained and transferred through the bypass channels from the upper chamber.

The dampening slot slows movement of the lower plunger so as to permit complete mixing of the diluent from the upper chamber with the dry medication in the lower chamber. The floating piston is forced from the dampening slot by the abutment of the upper piston against the lower piston. This occurs when all of the diluent fluid between the upper and lower plunger has passed through the ribbed by-pass portals into the lower chamber.

The length of the bypass portals is of any length greater than the length of the dividing piston, but not of such length as to encroach into the distal chamber of the auto-injection device, or of such length as prevent the putative lower chamber from receiving the required volume for exact reconstitution and tight resealing by the dividing piston.

Operationally, the adjustment mechanism is manipulated to select the appropriate settings (as shown be easily recognized non-volumetric indicia) that

corresponds to an individual's relevant parameter(s) (*i.e.*, age, height, weight). The adjustment mechanism can utilize a variety of known adjustors including, but not limited to, a dial. Once the device is set for the individual's parameter(s) (*i.e.*, patient size), the reconstitution mechanism is actuated so that the upper plunger pressurizes liquid in the upper chamber, causing the lower plunger to move downward and enter the by-pass mixing portals. The bypass portals, now opened and confluent to each side of the lower plunger, cause accelerated fluid flow from the upper chamber to mix and reconstitute the dry contents in the lower drug chamber. Alternatively, the reconstitution mechanism is actuated first and then the needle depth and/or dosage (based on a patient parameter) is selected.

Then, the distal end of the device of the subject invention is applied to an appropriate body area for intramuscular injection of the reconstituted medicament. In one embodiment, firm pressure applied to the distal end of the auto-injection device actuates a spring-loaded injector mechanism to advance a sterile needle into the patient's body to inject the chosen volume of liquid medicament. Alternatively, a trigger, if provided, located at the proximal end of the device can actuate the spring-loaded injector mechanism to advance a sterile needle into the patient's body to administer the appropriate dosage of medication to the patient.

One embodiment of the present invention provides a dual chamber auto-injection device **100**, as shown generally in FIGS. 3 and 4. The auto-injection device **100** has non-volumetric indicia **105** that correspond to medication dosages based on an individual's relevant parameters. The appropriate dosage, which can be adjusted continuously or discretely, are marked on a non-volumetric scale (*i.e.*, Broselow-Luten tape) affixed to the housing of the device **100**.

By rotating an adjustment knob **110** around its longitudinal axis, a user can select the appropriate dose of medication to be administered and/or needle penetration depth based on the patient's relevant parameters. A movable indicator **115** displays to the user a representation of the relevant parameter and appropriate dosage amount to be administered using the subject device **100**. The movable indicator **115** corresponds in movement to that of the adjustment knob **110**. A needle protector **120** is provided to protect the user from accidental needle punctures.

The auto-injection device **100** has a central longitudinal bore **140**. The bore **140** accommodates a tubular member **143**, to which is attached the movable indicator **115**. Movement of the tubular member **143** displaces the amount of medication to be reconstituted.

The auto-injection device **100** has a distal end **125** and a proximal end **130**. Distal end **125** can be provided with a needle **135** so that liquid contained within the syringe bore **140** can be discharged via the needle **135**.

The auto-injection device **100** also has an upper cylindrical section **145** having an upper chamber **150** for containing fluid and a lower cylindrical section **155** with a lower chamber **160**. The upper chamber **150** contains a liquid diluent **165**. Lower chamber **160** contains a dry medicine or drug **170**.

An enlarged diameter section **175** is provided in between the distal **125** and proximal **130** ends. The enlarged diameter section **175** has a cylindrical wall, a frustoconical wall, a second frustoconical wall, and a plurality of radially and longitudinally extending ribs **180**.

The ribs **180** have cutouts or recesses **185** that define in combination a dampening slot for receiving the periphery of a lower piston **190**. Each pair of ribs **180** defines a bypass flow channel. During use, the lower piston **190** registers in the dampening slot defined by recesses **185** so that the lower piston **190** is held by the recesses **185** until the liquid diluent **165** can flow via the bypass flow channels from upper chamber **150** into lower chamber **160**. There, it mixes with the dry drug **170**.

An upper piston **195** is positioned within the bore **140** next to the proximal end **125** of the device **100**. The lower piston **190** is positioned in between enlarged diameter section **175** and distal end **130**. In this fashion, the upper chamber **150** is formed in between lower piston **190** and upper piston **195**. The lower chamber **160** is that portion of syringe bore **110** below lower piston **190** or in between lower piston **190** and distal end **125** of the device **100**. The liquid diluent **165** contained in upper chamber **150** is separated from and sealed from the dry drug **170** in lower chamber **160**.

A first spring-loaded mechanism **200** is used to force the upper piston **195** and lower piston **190** from the proximal end **130** toward the distal end **125** of the device **100** to reconstitute the medicament to be delivered to the patient. The spring-loaded

mechanism **200** can be actuated using a variety of known methods including, but not limited to, a release button **205**.

Once the spring-loaded mechanism **200** is actuated, the lower piston **190** moves downwardly until the periphery of the lower piston **190** engages the correspondingly shaped recesses **185** of ribs **180**, which form a dampening slot to prevent further downward movement of the lower piston **190**. Simultaneously, the upper piston **195** also moves downwardly until the upper piston **195** engages the lower piston **190**. The upper and lower piston remain engaged until such time as the medicament is to be administered.

When the reconstituted medicament is to be administered, the distal end **125** of the device **100** is applied to the appropriate body area for injection. A trigger **213** located in the proximal end **130** of the device **100**, is then depressed to actuate a second spring-loaded mechanism **210** that forces both pistons **190, 195** to move downwardly so that the reconstituted drug product can be dispensed via needle **135** into the patient.

The auto-injection device of the present invention has an adjustment mechanism to adjust the dosage of the reconstituted drug product to be administered to a patient. Contact pressure of a threaded rod **215** causes the proximal end of the tubular member **143** (on which a moveable indicator **115** is located) to move toward the distal end **125** of the device. The threaded rod **215** forms the driven member of a spindle drive, configured to include the threaded rod **215** and a threaded sleeve **220**. The threaded sleeve **220** surrounds the threaded rod **215** as the drive member. To move the piston tubular member **143**, the threaded sleeve **220** together with the threaded rod **215** is advanced against an elastic return force by actuation of the adjustment knob **110**. The adjustment knob **110** in turn actuates the tubular member **143** to advance in the direction toward the distal end of the proximal enclosure **130**. The adjustment knob **110**, the drive members **215, 220**, and the tubular member **143** are linearly shifted along a common axis, the shifting axis, as indicated as a dot-dash in the figures. In this arrangement, the distance by which the adjustment knob **110** and the drive members **215, 220** are shifted on actuation is always the same. Thus, the distance covered by the tubular member **143**, as influenced by the drive **215, 220**, allows for variable selection of a dose of medication to be administered by injection.

All patents, patent applications, provisional applications, and publications referred to or cited herein are incorporated by reference in their entirety, including all figures and tables, to the extent they are not inconsistent with the explicit teachings of this specification.

It should be understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this application.

Claims

We claim:

1. An auto-injection device comprising non-volumetric indicia for at least one patient parameter, an indicator, a dosage adjusting means, and an adjustment mechanism.

2. The auto-injection device of claim 1, wherein the adjustment mechanism sets the dosage adjusting means based on the patient parameter.

3. The auto-injection device of claim 1, further comprising a needle depth adjusting means.

4. The auto-injection device of claim 3, wherein the adjustment mechanism simultaneously sets the dosage adjusting means and the needle depth adjusting means based on a patient parameter.

5. The auto-injection device of claim 2, wherein the patient parameter is selected from the group consisting of age, size, height, weight, and gender of the patient.

6. The auto-injection device of claim 5, wherein the patient parameter is age and the patient is a pediatric patient.

7. The auto-injection device of claim 1, wherein the non-volumetric indicia is selected from the group consisting of numbers, characters, and colors.

8. The auto-injection device of claim 1, wherein the non-volumetric indicia is a Broselow-Luten tape.

9. The auto-injection device of claim 1, further comprising a means for separation, and a reconstitution mechanism, wherein the means for separation separates different substances from contact with each other until such time as needed for administration.

10. The auto-injection device of claim 9, wherein the means for separation is two chambers created and separated by a dividing piston, wherein the dividing piton includes upper and lower plungers.

11. A method for injecting medication to a patient comprising:

a) assessing a patient parameter;

b) manipulating an adjustment mechanism on an auto-injection device comprising medicament, a distal end, a proximal end, a dosage adjusting means, non-volumetric indicia, an indicator, and the adjustment mechanism, wherein said non-volumetric indicia is based upon the patient parameter;

c) assessing indicator position against the non-volumetric indicia as the adjustment mechanism is manipulated;

d) once the indicator is positioned on the appropriate non-volumetric indicia based on the patient parameter, administering the medicament to the patient by actuating the auto-injection device to release the medicament out of the distal end of the device.

12. The method of claim 11, wherein the step of administering medicament to the patient comprises actuating the auto-injection device to release the medicament out of the distal end of the device to an intravenous line.

13. The method of claim 11, wherein the step of administering medicament to the patient comprises actuating the auto-injection device to release the medicament out of the distal end of the device into a body of the patient.

14. The method of claim 11, wherein the patient parameter is selected from the group consisting of age, size, height, weight, and gender of the patient.

15. The method of claim 11, wherein the non-volumetric indicia is selected from the group consisting of numbers, characters, and colors.

16. The method of claim 15, wherein the non-volumetric indicia is a Broselow-Luten tape.

17. The method of claim 11, wherein the auto-injection device further comprises a needle depth adjusting means, wherein manipulating the adjustment mechanism simultaneously sets the dosage adjusting means and the needle depth adjusting means based on the patient parameters.

18. The method of claim 11, wherein the auto-injection device further comprises a means for separation, a reconstitution mechanism, and at least two different substances that form the medicament, wherein the means for separation prevents the substances from contact with each other until such time as needed for administration.

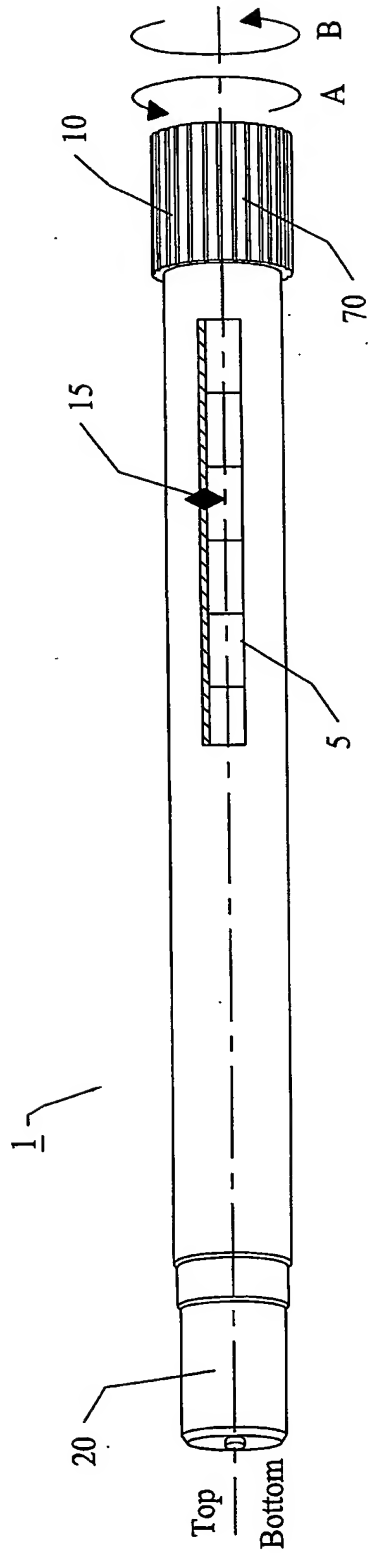


FIG. 1

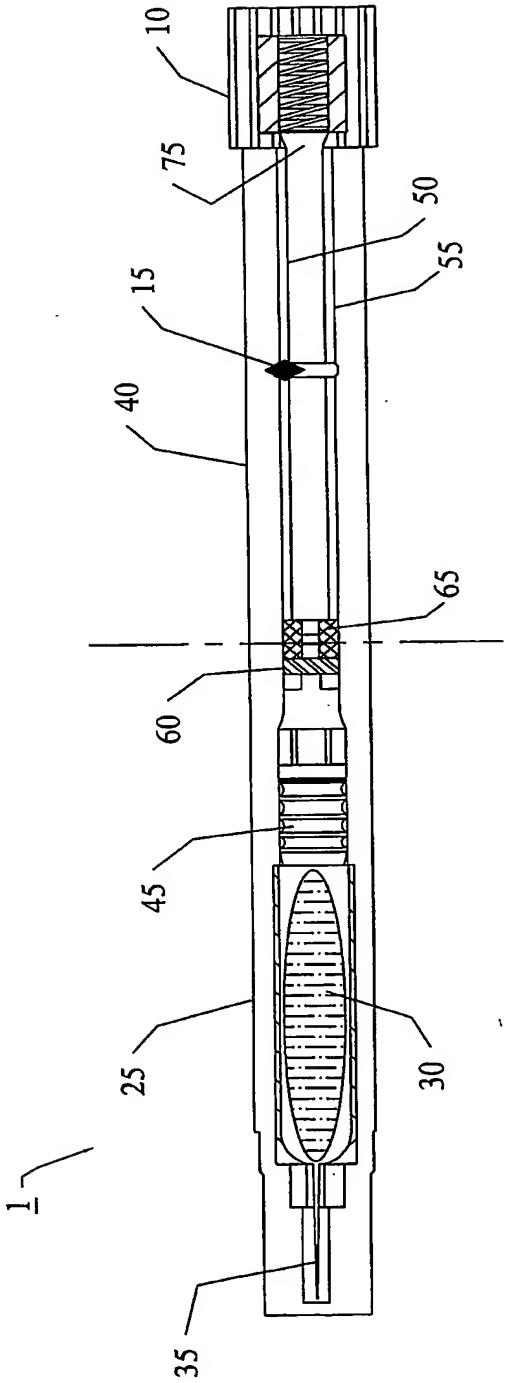


FIG. 2

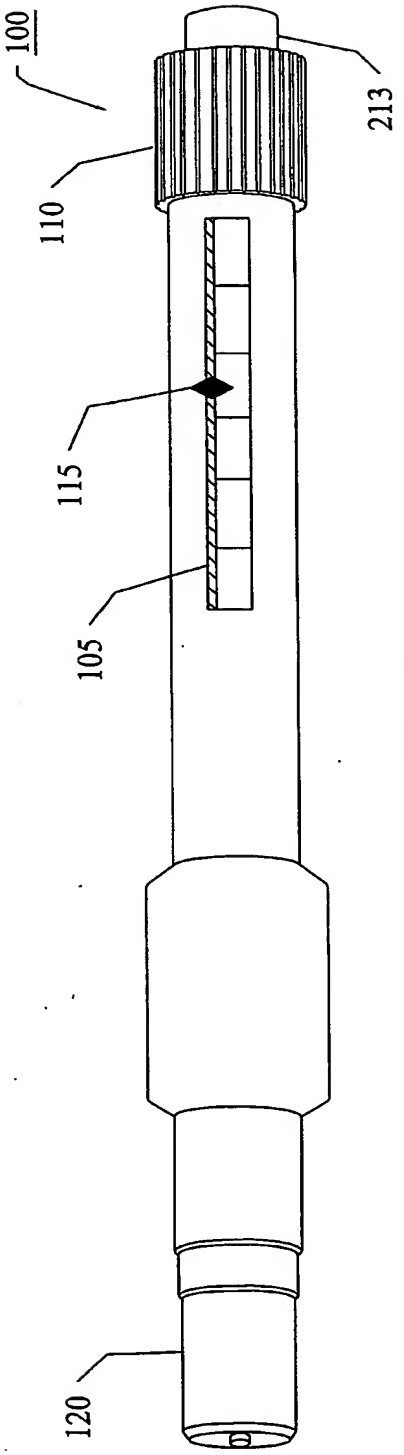

100
110
213
115
105
120

FIG. 3

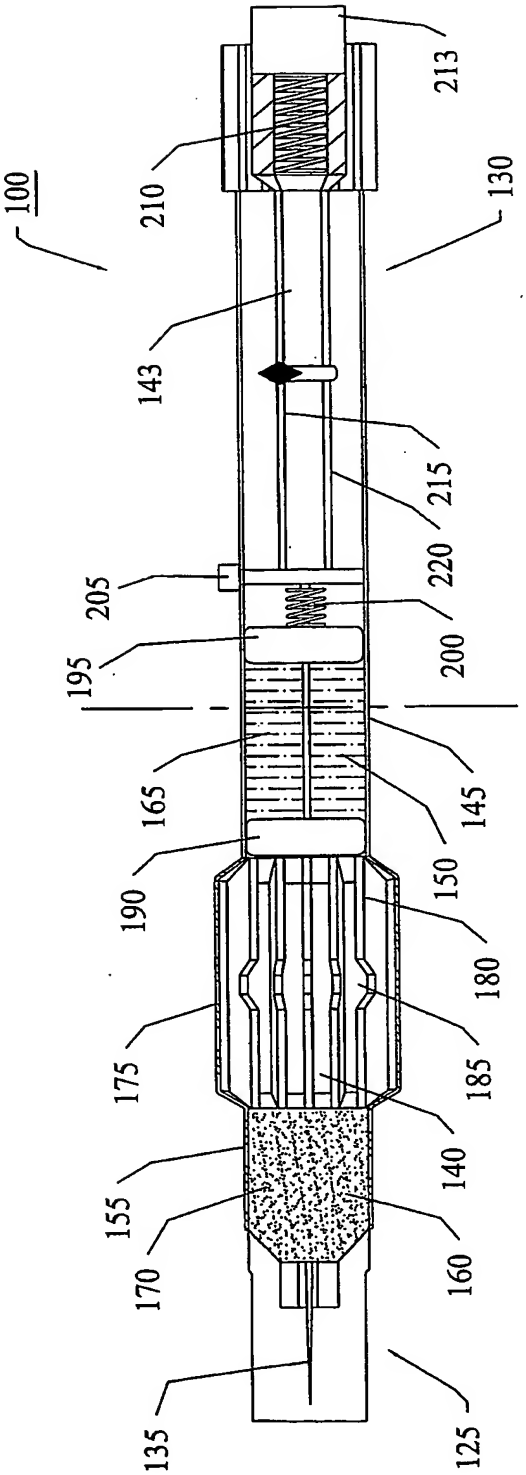

100
210
213
130
143
215
220
205
200
195
165
145
190
150
180
175
185
140
155
160
170
135
125

FIG. 4

INTERNATIONAL SEARCH REPORT

In ɔnal Application No
PCT/US2004/017959

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/315 A61M5/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M A61J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/74422 A (SCIENCE & TECHNOLOGY CORP & CO) 11 October 2001 (2001-10-11) page 10, line 9 - page 12, line 4; figures 1-4	1-10
Y	US 5 104 380 A (MARSHALL JEREMY M J ET AL) 14 April 1992 (1992-04-14) cited in the application column 2, line 65 - column 3, line 11; figure 1 column 4, line 41 - line 60	1-8
Y	WO 00/62839 A (BECTON DICKINSON CO ; DESALVO DAVID (US); GIAMBATTISTA LUCIO (US)) 26 October 2000 (2000-10-26) page 7, line 9 - page 11, line 21; figures 1-7	9,10

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 September 2004	01/10/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Björklund, A

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/017959

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 983 761 A (BROSELOW JAMES B) 8 March 2000 (2000-03-08) paragraph '0029! - paragraph '0032!; figures 1,2	1-10
A	DE 197 28 103 A (HEINICKE WINFRIED DR MED) 7 January 1999 (1999-01-07) column 2, line 48 - line 52; figures 1-3	3,4
A	WO 00/56384 A (BULL ANTHONY ERIC ; DUGMORE PETER BALFOUR (ZA); REYNOLDS STANFORD WILL) 28 September 2000 (2000-09-28) page 10, paragraph 2	3,4

INTERNATIONAL SEARCH REPORT

ational application No.
PCT/US2004/017959

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 11-18
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery. The claims define methods for injecting medication to a patient which clearly represents methods of treatment of the human or animal body by surgery.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/017959

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0174422 A	11-10-2001	US 6413241 B1	02-07-2002
		AU 5298401 A	15-10-2001
		WO 0174422 A1	11-10-2001
		US 2002087121 A1	04-07-2002
US 5104380 A	14-04-1992	AU 619536 B2	30-01-1992
		AU 3306489 A	19-10-1989
		BR 8901828 A	28-11-1989
		DE 68912814 D1	17-03-1994
		DE 68912814 T2	18-08-1994
		DK 186089 A	19-10-1989
		EP 0338806 A2	25-10-1989
		ES 2050792 T3	01-06-1994
		JP 2071758 A	12-03-1990
WO 0062839 A	26-10-2000	AU 4076000 A	02-11-2000
		EP 1171185 A2	16-01-2002
		JP 2002541929 T	10-12-2002
		WO 0062839 A2	26-10-2000
EP 0983761 A	08-03-2000	US 6132416 A	17-10-2000
		EP 0983761 A2	08-03-2000
DE 19728103 A	07-01-1999	DE 19728103 A1	07-01-1999
WO 0056384 A	28-09-2000	AU 3184200 A	09-10-2000
		WO 0056384 A1	28-09-2000